Lewis.

Studies On The Quantitative Estimation Of Alkaloids By Means Of Immiscible Solvents.

STUDIES ON THE QUANTITATIVE ESTIMATION OF ALKALOIDS BY MEANS OF IMMISCIBLE SOLVENTS

BY

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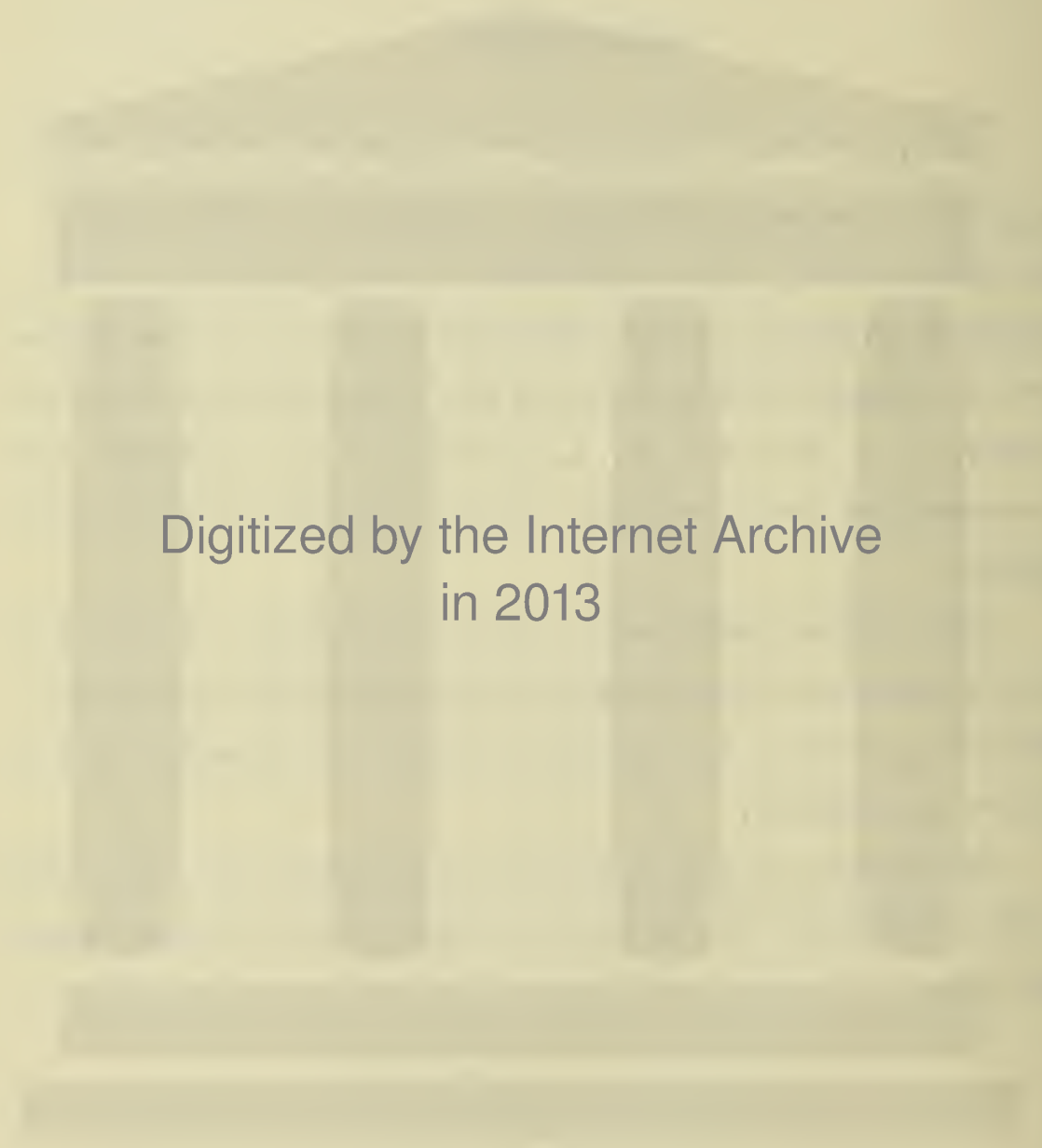

Table of Contents

THE QUANTITATIVE ESTIMATION OF ALKALOIDS BY THE SHAKING-OUT PROCESS.

1- Introduction: Discussion of the Problem.

One of the oldest and most widely used methods of alkaloidal assay is based upon the general principle that alkaloids themselves are quite insoluble in water and soluble in organic solvents, while their salts are soluble in water and insoluble in the organic solvents. The method of alkaloidal determination based upon this principle is known as the "shaking-out" process familiar through its connection with the Dragendorff (1) method of plant analysis and the Stas-Otto (2) poison assay. It is assumed that the alkaloidal salt is practically insoluble in organic solvents and the alkaloid insoluble in neutral aqueous solutions. It also assumes that the salt is neither hydrolysed by the aqueous solution nor decomposed by the organic solvent. Both Dragendorff and Otto certainly realized that the principles were not absolute. Dragendorff made exception to the rule in the cases of the almost quantitative estimation of caffeine, and the removal of traces of veratrine by benzene and of theobromine, colchicine, papaverine, narceine and traces of narcotine by chloroform from acid aqueous solution of the alkaloids. Otto recognized the fact that ether took up traces of colchicine, papaverine, narcotine, veratrine, and atropine from their acid solution.

In most alkaloidal assays of this type, the acid aqueous solution obtained by the extraction of the sample with dilute

acid is shaken out with the organic solvent in order to remove from the mixture those substances which might later appear with the alkaloid, causing inaccurate results in the assay. Such substances are coloring matter, essential oils, bitter principles, tannins, etc. After this the acid aqueous solution is made alkaline and shaken out with more immiscible solvent, removing the alkaloid in more or less pure condition. Purification is completed by shaking out this chloroform or ether solution with acid, making the acid solution alkaline and shaking out with more chloroform or ether. This is done several times. Finally the organic solvent is removed by evaporation and the residue determined by direct weight or by dissolving in standard acid and titrating the excess with standard alkali.

During the process, several sources of error are being introduced. In the first place, the alkaloidal salt may be slightly soluble in the organic solvent. There is also the possibility of the salt being hydrolysed by the water present into free alkaloid and acid. This free alkaloid would be easily soluble in the organic solvent. There are some cases known where the organic solvent either decomposes the alkaloid or else combines with it. These factors may cause a decrease in the amount of alkaloid in the acid solution with a corresponding decrease in the total alkaloid at the end of the assay. During the removal of the alkaloid from an alkaline solution by extraction with organic solvent, any insolubility of the alkaloid in the solvent and solubility in the alkaline solution will cause low results. This last, however is not a great source

of error except in the extraction of certain alkaloids with ether. And finally the shaking out of the alkaloidal solution in organic solvent introduces the problem of the possible insolubility of the salt formed in the acid solution, or if not its insolubility, its slow solubility. This is very apparent in the case of the salts of strychnine.

It is the purpose of this work, to obtain such results as will describe the partition of the alkaloid between the acid layer and the immiscible solvent, using different acids under different concentration conditions. In order to obtain more complete data, the equilibrium conditions were determined starting with an acid solution of the alkaloid and as well, shaking out the solution of the alkaloid in organic solvent with an acid. Thus it is hoped that the following conditions might be established for each alkaloid:

a- Which salt is most insoluble in chloroform and ether, and what concentration acid is most favorable to this condition.

b- Which acid and in what concentration removes the alkaloid most completely from its solution in chloroform and ether.

In order to put the results obtained in the form most quickly available, a new term, that of EXTRACTION FACTOR has been introduced and the factor calculated for the different sets of conditions obtained in the course of the research. By 'extraction factor' is meant the ratio of the amount of alkaloid in the layer of added solvent to the amount originally present in the first solution. For practical purposes, this would be a far better value to have than that of the partition

ratio or the sum of the partition ratios for the different alkaloidal molecular species present. The extraction factor shows at a glance the completeness of the extraction, an indication of the value of extraction under those conditions. The partition ratio tells only the partition of one molecular species between two layers of equal volume, by definition of the term 'partition ratio'.

II- Historical.

Attention was first called to the quantitative solution of the problem, through an article published by Dr. C. Kippenberger (3) in 1897. In this paper he states clearly the possibilities of error in alkaloidal estimation through hydrolysis of the salt with the subsequent solution of the free alkaloid. He suggests the use of chloroform or chloroform containing a little alcohol as solvents.

Three years later, Kippenberger (4) published a second paper in which he endeavored to establish the question on a firmer basis. He worked with the alkaloids Strychnine, Brucine, Atropine, Morphine, Aconitine, Veratrine, Papaverine, Narceine, Codeine, Emetine, Pelleteriene, Cocaine, Quinine, Narcotine, Coniine, Sparteine, Thebaine, Hyoscyamine, Daturine, Scopolamine and the base Caffeine. For shaking out he used chloroform and ether.

The action of the salts of the following acids was studied:

Hydrochloric Acid	21.9% HCl
Sulphuric Acid	40.1% H_2SO_4
Tartaric Acid	
Oxalic Acid	

In some cases, sodium chloride was added to the acid solution and its effect observed.

The alkaloid was dissolved with an excess of acid in 70 cc of water and 50 cc of the immiscible solvent added. This mixture was shaken in a separatory funnel for about three minutes. After fully clearing, the layers were separated and

the chloroform or ether layer washed with a few cc of water. The organic solvent was then evaporated on a water bath and the residue, alkaloid plus alkaloidal salt, dried over concentrated sulphuric acid. The amounts of alkaloid and alkaloidal salt present were determined in the following manner; the residue was dissolved in an excess of N/50 standard acid and the excess acid titrated back with N/50 standard alkali. This value for acid neutralized by alkaloid indicated the amount of free alkaloid present in the residue. The solution was then made alkaline with a slight excess of sodium hydroxide and extracted again with chloroform. The amount of total alkaloid was obtained by evaporation of the solvent and solution of the residue in standard acid with titration for excess acid as before. Subtraction of the first value, that of the free alkaloid from the second, or total alkaloid value will give the amount of alkaloid present in the residue as salt.

The results are found in the following tables. The column containing the strength of acidity was compiled by the author of this paper , from the data of Kippenberger.

Table 1. Kippenberger.

Extraction of an alkaloid by chloroform from its solution in hydrochloric acid.

Alkaloid Soln in 70cc Water	Amount Alk. 50cc $CHCl_3$.	Indicator	Strength Acid	Alkaloid Free	Alkaloid Salt
0.2g Strychnine	0.0910	Azolitmin	0.15N	0.0114	0.0806
" Brucine	0.0798	"	0.075N	0.0056	0.0742
" Atropine	0.0014	"	"	-	-
" Morphine	-	"	"	-	-
" Aconitine	0.0971	"	0.03N	0.0158	0.0813
" Veratrine	0.0807	"	0.075N	0.0077	0.0730
" Codeine	Trace	"	0.03 N	-	-
" Cocaine	0.0021	"	0.015N	-	-
" Quinine	Trace	"	0.03 N	-	-

Table 2. Kippenberger.

Extraction of an alkaloid by chloroform from its solution in sulphuric acid.

0.2g Strychnine	Trace	Azolitmin	0.17N	-	-
" Brucine	0.0020	"	"	-	-
" Atropine	-	"	0.034N	-	-
" Morphine	-	"	"	-	-
" Aconitine	0.0120	"	0.017N	0.0120	-
	0.0064	"	0.085N	0.0064	-
	Trace	"	0.255N	-	-
" Veratrine	Trace	"	0.017N	-	-
" Codeine	-	"	0.034N	-	-
" Quinine	-	"	"	-	-

Table 3. Kippenberger.

Extraction of an alkaloid by chloroform from its solution in a mixture of hydrochloric acid and sodium chloride.

Alkaloid Soln in 70cc Water	Amount Alk. 50cc $CHCl_3$.	Indicator	Strength Acid	Alkaloid Free	Alkaloid Salt
0.2g Atropine 14cc NaCl	0.0192	Azolitmin	0.075N	-	Trace
" "	0.0149	"	0.015N	-	"
" Quinine 14cc NaCl	0.0100	Haematoxylin	0.03 N	0.0037 acid salt 0.0063 neutral salt	
" Aconitine 14cc NaCl	0.2160	Azolitmin	0.017N	0.0306	0.1854
" Quinine	0.0057	Haematoxylin	0.03N	0.004 acid salt 0.0017 neutral salt	

Table 4. Kippenberger.

Extraction of an alkaloid by chloroform from its solution in tartaric acid.

0.2g Strychnine 0.4g Tartaric Acid	0.0020	Azolitmin		-	-
" Brucine 0.4g Tartaric Acid	0.0032	"		-	--

Table 5. Kippenberger.

Results of shaking out the acid alkaloidal solution with ether, under the same conditions as before.

From Hydrochloric Acid solution.

Ether took up:

Narcotine ---- 0.0002 grams.
Caffeine ---- 0.0112 grams, as free caffeine.

The following were found in noticable traces:

Aconitine, Narceine, and Emetine.

None of the other alkaloids gave up a trace to ether.

From Sulphuric Acid solution.

Ether took up:

Caffeine ---- 0.0083 grams as free caffeine.

The following were found in noticable amounts:

Aconitine, Papaverine, Narceine, Emetine and Narcotine, also very slight traces of Veratrine, Strychnine, and Codeine.

The addition of sodium chloride to the solutions gave the following results:

a- From Hydrochloric Acid in noticable traces; Narcotine, Atropine, and Quinine.

b- From Sulphuric Acid solution; Aconitine.

Ether removed neither Brucine nor Strychnine from tartaric acid solutions.

In 1901, Hans Proelss (5) gave a short description of the behavior of alkaloidal solutions toward different solvents. The work was divided in two parts; the first to determine the best solvent for the alkaloids as a class, and the second, the best solvent for the individual alkaloids. He compared the relative extractive powers of ether, chloroform, and benzene, and also mixtures of ether and chloroform, and alcohol and chloroform, for the alkaloids; Picrotoxin,

Veratrine, Strychnine, Atropine, Codeine, and Morphine. His method consisted in dissolving 0.1 gram of alkaloid in 50 cc of water containing a few drops of hydrochloric acid. After making alkaline with sodium carbonate, the aqueous solution was extracted three times with the solvent. He states that constant results could not be obtained of sufficient accuracy to be anything more than comparative.

1- The best solvent for alkaloids in general.

Solvent		Results
Ether	Very good with	Colchicine, Brucine.
Chloroform	" " "	Colchicine, Brucine, Digitalin, Veratrine, Atropine, Strychnine.
Chloroform and ether	" " "	Colchicine, Atropine, Veratrine, Picrotoxin.
Chloroform and alcohol	" " "	Colchicine, Veratrine, Digitalin, Atropine, Codeine, Morphine plus acid potassium carbonate.
Benzene	"" " "	Colchicine, Strychnine, Atropine, Codeine, Picrotoxin.

In conclusion he states that the best shaking-out liquid for alkaloids in general is chloroform, because of the solubility of most of the alkaloids in chloroform.

2- The best shaking-out liquid for the individual alkaloids.

Alkaloids	Results
Atropine ----------	Any solvent satisfactory.
Brucine ----------	Same as for Picrotoxin.
Codeine ----------	Alcohol plus chloroform, benzene.
Colchicine ----------	Any solvent satisfactory.
Morphine ----------	Alcohol plus chloroform from potass-

ium carbonate solution.

Picrotoxin --------- Ether, chloroform from sodium carbonate-ammonium hydroxide solution.

Strychnine --------- Chloroform, alcohol plus chloroform, benzene from sodium carbonate- ammoniacal solution.

Veratrine ---------- Chloroform, ether plus chloroform, ether and benzene from ammoniacal solution.

In conclusion, he states that emulsions form easiest with benzene and least with ether.

Ed. Springer (6) in 1902, studied the effect of the of the solvent chloroform on the extraction of the following alkaloids; Morphine, Coniine, Narcotine, Strychnine, Quinine, Codeine, Veratrine, and Cocaine, from solutions made acid with sulphuric, phosphoric, hydrochloric, tartaric, acetic, oxalic and citric acids.

The amount of alkaloid in the residue after evaporation of chloroform was determined by titration in the same way that Kippenberger did. For some reason, he was unable to obtain check results and so his work is of no value from a quantitative standpoint.

The following are his results:

Aconitine

Aconitine is removed as the salt from hydrochloric acid and as the pure salt in traces from the sulphuric acid solution.

Atropine

From hydrochloric acid, traces were removed as the salt, from sulphuric acid, traces as the free alkaloid; traces were found from the tartaric acid solution, also.

Cocaine

Some alkaloid is extracted from sulphuric and hydrochloric acid solutions, where the acid is present in small concentration.

Codeine

Codeine is not found in the chloroform residues from extraction of solutions of the alkaloid in phosphoric, tartaric, oxalic, citric, and sulphuric acids, although in the last case it was found that if the concentration of the acid was low enough, some of the alkaloid would be removed as the free base.

Morphine, Coniine, and Nicotine.

No alkaloid was extracted from solutions made acid with the following acids; hydrochloric, sulphuric and phosphoric.

Narcotine

Narcotine is removed from both hydrochloric and sulphuric acid solutions, partly as base and partly as salt.

Quinine

No alkaloid is removed from solutions of the sulphate, tartrate or phosphate. Some quinine is removed as the hydrochloride.

Strychnine

About 25 per cent was removed from the hydrochloric acid solution as the salt. Slight traces were removed from the other acid solutions.

Veratrine

Veratrine is removed in traces in solutions containing

small amounts of tartaric, sulphuric, and citric acids but such is not the case with large excess of sulphuric or phosphoric acids.

From this, it may be drawn that chloroform is a "good solvent" for the hydrochloric acid salts of the alkaloids. The solubility of the hydrochlorides is so great, in fact, that if in excess of acid the salt is taken over completely as the salt and only in the case of the weak base Narcotine, could traces of the free alkaloid be found, in the chloroform extract.

From the table, one would expect to find in the chloroform extract from the sulphuric acid solution in the Dragendorff assay, Aconitine and Narcotine, as well as the alkaloids mentioned by Dragendorff himself. Strychnine, Veratrine and Atropine might also be found in small amounts.

In 1906, Simmer (7) published an important paper on this subject. The work was divided in three parts:

1- The behavior of the salts of the common alkaloids toward extraction by chloroform and other important solvents.

2- The appearance of decomposition through treatment with chloroform.

3- The reducing action of the alkaloids.

Simmer prepared an aqueous solution of the alkaloidal salt, containing 0.2 gram or the free alkaloid to 50 cc of solution or 0.4 per cent of the free alkaloid. He then acidified with the different acids until he obtained the desired concentrations. Simmer neglected to state definitely the amount of chloroform used in the extraction but the general tone of the

paper would lead one to believe that he used equal amounts of chloroform and aqueous solution. These were mixed and the extraction carried on for an hour. At the end of the time, the layers were divided and the chloroform evaporated. The amount of free alkaloid and alkaloidal salt were determined in the residue in the usual manner.

It will be seen from the tables that many neutral salts are extracted by both chloroform and benzene; this is especially true in the cases of the salts of the nitric and halogen acids.

With strychnine hydrochloride, the least amount of salt is extracted from the neutral solution and the most from the solution that contains a 10 per cent excess of acid; the 25 per cent acid gives up less alkaloid than the ten per cent solution.

The behavior of the weak bases Colchicine, Caffeine, Narcotine, Papaverine, and Antipyrine is different. In strong hydrochloric acid solution of Colchicine, there is as much alkaloid removed by the chloroform as from the aqueous solution. The same is true with sulphuric or phosphoric acid solutions. Acids have very little effect on fixing Caffeine. Thebaine and Narcotine are removed from weak tartaric acid solutions as easily as from stronger acid solutions. Papaverine, Narcotine, and Thebaine are removed simply as salts and not as free bases.

Table 1. Simmer.

Behavior of Neutral and Acidified Alkaloidal Salt Solutions toward Extraction with Chloroform.

Alkaloidal Salt	Amount in 50 g Water	Strength Acid %	Grams Alkaloid Total	Free	Salt
Strychnine Hydrochloride	0.2377	0.0	0.0153	0.0142	0.0016
	"	0.1	0.0083	0	0.0083
	"	1.0	0.0250	0	0.0250
	"	10.0	0.0559	0	0.0559
	"	25.0	0.2330	0	0.2330
Strychnine Hydrobromide	0.2480	0.0	0.0200	0.0133	0.0067
	"	0.1	0.0167	0	0.0167
	"	1.0	0.0350	0	0.0350
Strychnine Hydriodide	0.2760	0.0	0.0560	0.0250	0.0317
Strychnine Nitrate	0.2377	0.0	0.0283	0.0233	0.0050
	"	1.0	0.0350	0	0.0350
Strychnine Sulphate	0.2610	0.0	Trace		
	"	1.0	"		
Veratrine Hydrochloride	0.2110	0.0	0.0530	0.0499	0.0031
	"	0.1	0.0327	0	0.0327
	"	10.0	0.1248	0	0.1248
Veratrine Nitrate	0.2200	0.0	0.0405	0.0405	0
	"	1.0	0.0811	0	0.0811
Veratrine Sulphate	0.2150	0.0	0.0374	0.0374	0
	"	0.1	Traces		
Veratrine Tartrate	0.2230	0.1	0.0842	0.0842	0
	"	2.0	0.0155	0.0155	0
	"	5.0	Traces		
Morphine Hydrochloride	0.2470	0.0	0.0045	0.0045	0
	"	0.1	0	0	0
	"	5.0	0	0	0

Table 1. Simmer. (cont)

Alkaloidal Salt	Amount in 50g Water	Strength Acid %	Grams Alkaloid Total	Free	Salt
Morphine Sulphate	0.2500	0.0	0.0037	0.0037	0
	"	0.1	0	0	0
Morphine Acetate	0.2630	0.0	0.0197	0.0197	00
Codeine Hydrochloride	0.2340	0.0	0.0371	0.0371	0
	"	0.1	0.0015	0	0.0015
	"	10.0	0.0079	0	0.0079
Codeine Hydrobromide	0.2620	0.0	0.0126	0.0126	0
	"	0.1	Traces		
	"	10.0	0.0110	0	0.0110
	"	25.0	0.0079	0	0.0079
Codeine Sulphate	0.2470	0.0	0.0276	0.0276	0
	"	0.1	Traces		
Codeine Tartrate	0.2360	0.1	0.0110	0.0110	0
Codeine Citrate	0.2480	0.0	0.0395	0.0395	0
	"	0.1	0.0158	0.0158	0
Cocaine Hydrochloride	0.2240	0.0	0.0490	0.0490	0
	"	0.1	0.0037	0.0015	0.0022
	"	1.0	0.0045	0	0.0045
	"	10.0	0.0075	0	0.0075
Cocaine Sulphate	0.2640	0.0	0.0143	0.0143	0
	"	0.1	Traces		
Cocaine Tartrate	0.2310	0.0	0.0543	0.0543	0
	"	0.1	0.0528	0.0528	0
	"	1.0	0.0332	0.0332	0
	"	5.0	0.0015	0.0015	0
Atropine Hydrochloride	0.2250	0.0	Traces of free Atropine		
	"	0.1	" " "		"
	"	10.0	0.0028	0	0.0028

Table 2. Simmer.

Behavior of Neutral and Acidified Alkaloidal Salt Solutions toward Extraction with Benzene.

Alkaloidal Salt	Amount in 50 g Water	Strength Acid %	Grams Alkaloid Total	Free	Salt
Strychnine Hydrochloride	0.2377	0.0	0.0075	0.0075	0
	"	0.1	0	0	0
	"	1.0	0	0	0
	"	10.0	Traces		
Strychnine Hydrobromide	0.2480	0.0	0.0033	0.0033	0
	"	0.1	Traces		
Strychnine Hydriodide	0.2760	0.0	0.0033	0.0033	0
Strychnine Sulphate	0.2610	0.0	0	0	0
Strychnine Nitrate	0.2377	0.1	Traces		
Veratrine Sulphate	0.2150	0.0	Traces		
	"	0.1	"		
Codeine Hydrochloride	0.2340	0.0	0.0055	0.0055	0
	"	0.1	0	0	0
	"	10.0	0	0	0
Codeine Hydrobromide	0.2620	0.0	0.0023	0.0023	0
	"	1.0	0	0	0
Codeine Sulphate	0.2470	0.0	0.0031	0.0031	0
Codeine Citrate	0.2480	0.0	0.0023	0.0023	0

2- The decomposing power of the alkaloids on chloroform.

The observation had been made by many authors that extraction of the alkaloids with chloroform is attended with a decomposition of the chloroform, giving rise to free hydrochloric

acid.

In order to determine this, Simmer extracted a mixture of 50 grams of water and 2 grams of finely powdered alkaloid with 50 grams of chloroform for eight hours. First the water was tested. This always gave an opalescence with silver nitrate but showed itself to be free from alkaloid, except in the few cases due to the relative insolubility of the alkaloid in chloroform. The chloroform layer was then evaporated and the residue dissolved in water containing a sufficient amount of sulphuric acid. Silver nitrate solution was then added. When a definite precipitate was observed, this was filtered, dissolved in ammonia and precipitated again with nitric acid. Then the pure precipitate was filtered in a Gooch crucible and weighed.

The following results were obtained:

Alkaloid 2gms	AgCl from the chloroform layer	Corresponding to HCl	Alkaloid
Atropine	0.0038	0.0009	0.0072
Brucine	0.0138	0.0033	0.0333
Quinine	Traces		
Cinchonidine	"		
Cinchonine	"		
Cocaine	0.0021	0.0005	0.0042
Codeine	Traces		
Morphine	0		
Narcotine	0		
Nicotine	Traces		
Strychnine	0.0035	0.0008	0.0073
Veratrine	0.0043	0.0010	0.0173

Thus we see that the action of the alkaloid upon the chloroform is negligible, except in the cases of Brucine and Veratrine.

Marden and Elliott (8) in 1914 published a paper on the methods of extraction by immiscible solvents from the point of view of the distribution ratios. They shook out the alkaloids Aconitine, Atropine, Codeine, Coniine, Morphine, Quinine, and Strychnine with the solvents chloroform and ether. Ammonium hydroxide was used to make the acid solution alkaline.

From the distribution coefficient and a certain subsequent algebraic calculation, they could determine the number of extractions necessary to remove 99.9% of the alkaloid. The distribution ratio (d) is indicated by the expression

$$\frac{\text{Concentration in 10 cc of water}}{\text{Concentration in 10 cc of non-aqueous solvent}} = \frac{C}{C'} = (d)$$

The algebraic expression for the calculation of the number of shakings necessary for an extraction is indicated by

$$\frac{x_n}{x_o} = \left(\frac{da}{e+da}\right)^n \quad \text{where}$$

a = volume of the aqueous solvent,

e = volume of non-aqueous solvent,

d = distribution ratio,

x_o = original amount of material to be extracted in the aqueous layer,

x_n = amount of material in the water layer after n extractions.

Aconitine

In the system Aconitine, ether and aqueous ammoniacal solution, using 100 cc water, 5 cc ammonium hydroxide, and 50 cc

of ether, the following result was obtained, d = 0.140; but on substituting 30 cc of chlororform for the 50 cc of ether, the value of d became 0.017.

Atropine

The distribution ratio in the system water and chloroform was found to be very small and three extractions with 10 cc of chloroform from 50 cc of the aqueous solution were found sufficient to remove the atropine.

Codeine

In the system, 100 cc water, 5 cc ammonium hydroxide, and 50 cc ether, (d) had a value, 0.939. If 30 cc chloroform were substituted for the ether, the value became 0.0067.

Coniine

Owing to the volatility of the coniine, it was very difficult to get the partition ratio.

Morphine

In the system, saturated aqueous solution of potassium carbonate and a mixture of methyl alcohol and chloroform, (d) possessed a value of 0.154 with variations from 0.200 to 0.127. The value for the system, 100 cc water, containing 35 grams sodium chloride, and 45 cc of a 2:1 mixture of chloroform and ethyl alcohol was found to be 0.528.

The value for (d) between water and chloroform- amyl alcohol mixture was 0.345.

Quinine

Between water made alkaline with ammonium hydroxide, and chlororform, quinine was found to possess such a low distribution

coefficient that three washings of a 50 cc aqueous solution with 10 cc or chloroform were found to remove all of the alkaloid.

Strychnine

The authors determined the distribution coefficients for systems containing chloroform alone and in a mixture with ether in order to see which would prove more efficient, as there has been a great difference or usage.

For the system, 100 cc of water, 2 cc of ammonium hydroxide, and 30 cc or chloroform, (d) was found to be equal to 0.003, but on substituting a mixture or 1:3 chloroform and ether, the value 0.087 was obtained.

Summary of the Historical Chapter.

In looking over the work that has been published on the subject of the quantitative estimation of the alkaloids by the shaking-out process, sufficient data will be found to establish the equilibrium conditions of the systems, alkaloidal hydrochlorides or sulphates between their acid solutions and chloroform or ether. Results are lacking, however, which will show the partition of alkaloidal tartrates between tartaric acid and those solvents.

In addition the whole subject of the extraction of an alkaloid from its solution in chloroform by an acid has never been investigated. If equilibrium is reached, this should give the same value as with the extraction of the acid salt solution by that solvent. In practice, it takes a long time with some of these systems and there are certain other factors entering in.

III- Theoretical Considerations.

In an acid solution of a neutral alkaloidal salt, the following equilibria are established;

a- The alkaloidal salt is in equilibrium with the free alkaloid and acid due to the hydrolysis of the salt, and

b- The neutral salt and acid are in equilibrium with an acid salt. It is possible that more than one acid salt may be formed, in which case there will be as many more equilibrium reactions as there are acid salts formed. If chloroform is added to this system, and the mixture shaken, each of these equilibria may be affected. For example, the mass law equation for the hydrolysis of an alkaloidal salt, is expressed by the following,

$$\frac{C_{alkaloid} \times C_{acid}}{C_{salt}} = k,$$ where k is the mass law constant. The removal of one of the constituents will cause a resultant shift in the other concentrations in order that k may remain constant. The presence of a great excess of acid will drive back the hydrolysis by increasing the value for the term, C_{acid} with the resultant decrease in value for the term, $C_{alkaloid}$. At the same time, solution of the alkaloid in chloroform will cause a decrease in the value, $C_{alkaloid}$ with a resultant further lowering of C_{salt} in order to restore equilibrium. This salt which is removed is hydrolysed. So the result of the removal of free alkaloid is to increase the hydrolysis. Thus in this system at equilibrium, the conditions

existing are a resultant of these two equilibria which are progressing with opposite tendencies.

To approach the equilibrium from the other direction however, introduces a new factor, namely the speed of solution of the newly formed salt in the acid solution. This is the case when the alkaloid itself is dissolved in chloroform and shaken out with acid solution at ordinary temperatures. Where the acid is monobasic, the first result of the reaction is probably the formation of a neutral salt. In an excess of acid, the acid salt is then formed.

In the case of the dibasic acids, such as tartaric acid or sulphuric acid, the acid salt is first formed, similarly to the mechanism of the neutralization of sulphuric acid with sodium hydroxide. As more alkaloid combines, there is a gradual change from the acid salt into the neutral salt. The neutral salt in many cases seems to be very slowly soluble at ordinary temperatures, although it goes easily into solution at boiling temperature. With the excess of acid, however, the first acid salt is formed which is only slightly soluble in a small excess of acid, in some cases. As an excess of acid is added in larger amounts, the soluble higher acid salts are formed. Thus the solution in acid may be hastened by shaking out with fresh portions of the acid, in order to get the higher acid salts. This situation would not be met with where the salt solution is shaken with chloroform or ether, for in these cases, the salt is dissolved at a much higher temperature and the solution cooled.

IV- Experimental.

a) Preparation of some alkaloidal tartrates and a brief description of their properties.

The neutral salts were prepared by dissolving the alkaloids in an aqueous acid solution, containing equivalent amounts of tartaric acid in a large excess of water, at the boiling temperature. In the excess of hot water, the acid salt which forms first stays in solution and the remainder of the alkaloid completely neutralizes it. On cooling the solution slowly, the neutral salt comes out in beautiful crystals. In one or two cases, it was necessary to evaporate some of the solvent water in order to get the right concentration for crystallization.

The mon-acid salt may be prepared by dissolving the alkaloid in a slight excess of acid, in a small quantity of hot water. On cooling the crystals of the acid salt will come out.

These salts are further purified by crystallization from water several times.

In this way the crystalline salts of Brucine, Cinchonine, Cinchonidine, Quinine, Morphine, and Strychnine were prepared. The alkaloids Aconitine, Atropine, Cocaine, Codeine, and Veratrine were obtained in the form of tartrates for further investigation by simply dissolving the alkaloids in the proper concentration of acid, as their tartrate salts were amorphous.

The neutral salts are characterized as follows:

Strychnine.

M. P. 226°-227°, browning at 215°

Crystalline form: beautiful white rosettes.

Analysis 81.68% Strychnine
15.00% Water

Theoretical for $(C_{21}H_{22}N_2O_2)_2C_4H_6O_6.8H_2O$.

81.66% Strychnine
15.20% Water

Brucine

M. P. 236°-237°, with decomposition; browns at 210°.

Crystalline form: white cubes

Analysis 83.2 % Brucine
9.1 % Water

Theoretical for $(C_{23}H_{26}N_2O_4)_2\ C_4H_6O_6.5H_2O$.

83.7 % Brucine
8.8 % Water

Quinine

M. P. 199°, with browning.

Crystalline form: fine white needles.

Analysis 81.28% Quinine
2.56% Water

Theoretical for $(C_{20}H_{24}N_2O_2)_2\ C_4H_6O_6.\ H_2O$.

81.20% Quinine
2.3 % Water

Cinchonidine

M. P. 230°-231° with decomposition; browns at 218°.

Crystalline form: long white needles.

Analysis 79.68% Cinchonidine
4.60% Water

Theoretical for $(C_{19}H_{22}N_2O)_2\ C_4H_6O_6\ 2H_2O$.

79.69% Cinchonidine
4.64% Water

Cinchonine

M. P. 190° without either decomposition or browning.

Crystalline form: short white needles.

Cinchonine (continued)

Analysis	79.76%	Cinchonine
	2.8 %	Water

Theoretical for $(C_{19}H_{22}N_2O)_2\ C_4H_6O_6 \cdot H_2O$.

79.69%	Cinchonine
2.4 %	Water

The water of crystallization was determined by weighing the sample, heating at 110° to constant weight, and then dissolving the anhydrous salt in water. The solution was made alkaline and extracted twice with an excess of chloroform. The chloroform was evaporated and the residue heated to constant weight. The value obtained was that of the weight of the alkaloid in the sample of salt taken. From the value of alkaloid and that of water of crystallization was calculated the formula of the salt. The one exception in this proceedure was in the case of brucine where the residue from the chloroform extraction of the alkaline brucine solution was dissolved in standard acid and the excess acid titrated back with standard alkali.

The acid salts were analysed in the same manner.

b) Determination of the equilibrium conditions for the partition of the alkaloids and alkaloidal salts between aqueous neutral and acid solutions and an immiscible solvent (chloroform or ether).

1- Extraction of the neutral or acid aqueous alkaloidal solution with chloroform and ether.

0.2 gram of the neutral alkaloidal salt was dissolved in 25 cc of the aqueous acid solution of a definite concentration. To this were added 20 cc of chloroform or ether, and the mixture was shaken in a Jena Erlenmeyer flask for two hours and a half, at a temperature of 25°. The shaking was carried out in a water thermostat, accurate to within a tenth of a degree. The time of shaking was chosen after experiments were carried out to determine the time required for the reaction to come to equilibrium. It was found that in the case of strychnine tartrate, only half this time was required.

When that time had elapsed, the flasks were removed, the layers at once separated, and the chloroform or ether layer put in a small separatory funnel. After standing for about 10 minutes in order to make a clear separation, 10 cc of the chloroform solution were measured into a porcelain casserole, and the chloroform evaporated on a steam bath. The residue was taken up in 10 cc of N/50 sulphuric acid, and the excess acid titrated back with standard N/50 potassium hydroxide. Such indicators were used as would give the most accurate results for the individual alkaloids. The selection of indicator was made after reference to Kippenberger's table (9).

The value obtained in this way gave the amount of free alkaloid present in the residue. The neutral solution is made alkaline and extracted with chloroform. After separation, the solvent is evaporated and the residue again taken up in standard acid and titrated back with standard alkali. This gives the value for the total alkaloid. By subtracting the first value from the second, the amount of alkaloid present, combined with acid in the form of a salt, was obtained.

With Morphine, a slightly different procedure was carried out. In determining the amount of total alkaloid, the neutral solution after the first titration was made alkaline with ammonium hydroxide, since sodium and potassium hydroxide form salts with Morphine which are soluble in alkaline solution. The alkaline solution was then extracted with amyl alcohol, until it showed the absence of alkaloid, amyl alcohol being the best solvent for Morphine which will answer the purpose.

The solutions of the neutral salts were of the following acid strengths; neutral, N/8, N/4, N/2. The equilibrium conditions were determined for the tartrate salts of the alkaloids Aconitine, Atropine, Cinchonidine, Cinchonine, Cocaine, Codeine, Quinine, Morphine, Strychnine and Veratrine, in tartaric acid solutions. The equilibrium conditions for the solutions of alkaloidal sulphates in sulphuric acid and the hydrochlorides in hydrochloric acid were worked out with the idea of supplementing and adding to those values obtained by Kippenberger and Simmer. Table A gives the results of the extraction of the

salt solutions by chloroform and Table B, the values obtained by the extraction with ether.

Table A.

Alkaloid	Acid	Strength	20 cc Chloroform Grams Alkaloid Total	Free	Salt	Indicator
Strychnine	HTr	N/2	0	0	0	Azolitmin
	"	N/4	0	0	0	"
	"	N/8	0.0104	0.0104	0	"
	"	Neut.	0.0126	0.0114	0.0016	"
	Sulph.	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	N/50	0	0	0	"
	"	Neut	0.0127	0.0127	0	"
	HCl	N/2	0.0522	0	0.0522	"
	"	N/4	0.0424	0	0.0424	"
	"	N/8	0.0394	0	0.0394	"
		Neut.	0.0085	0.0081	0.0005	"
Brucine	HTr	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0.0026	0.0026	0	"
	"	Neut.	0.0076	0.0076	0	"
	Sulph.	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0.0143	0.0143	0	"
Cinchonidine	HTr	N/2	0.0012	0.0012	0	"
	"	N/4	0.0024	0.0024	0	"
	"	N/8	0.0018	0.0018	0	"
	"	Neut.	0.0024	0.0024	0	"
	Sulph.	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0.0086	0.0086	0	"
Cinchonine	HTr	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0.0016	0	0.0016	"
Caffeine	Sulph.	N/2	0.1928	0.1928	0	wt. of residue
	"	N/4	0.1930	0.1930	0	"
	"	N/8	0.1300	0.1300	0	"
	"	Neut.	0.1032	0.1032	0	"

Table A. (continued)

Alkaloid	Acid	Strength	Grams alkaloid in 20cc Chlororform Total	Free	Salt	Indicator
Cocaine	HCl	N/2	0	0	0	Cochineal
	"	N/4	0	0	0	"
	"	N/8	0.0432	0.0432	0	"
	"	Neut.	0.0432	0	0.0432	"
Codeine	HTr	N/2	0	0	0	Azolitmin
	"	N/4	0	0	0	"
	"	N/8	0.0018	0.0018	0	"
	"	Neut.	0.0046	0.0046	0	"
Quinine	HTr	N/2	0.0014	0	0.0014	"
	"	N/4	0.0028	0.0014	0.0014	"
	"	N/8	0.0028	0.0014	0.0014	"
	Neutral salt but slightly soluble in water					
	Sulph.	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0	0	0	"
Aconitine	HTr	N/2	0	0	0	Cochineal
	"	N/4	0.0537	0	0.0537	"
	"	N/8	0.0099	0	0.0099	"
	"	Neut.	0.0236	0.0136	0.0099	"
Atropine	HTr	N/2	0	0	0	"
	"	N/4	0.0036	0.0036	0	"
	"	N/8	0.0038	0.0010	0.0028	"
	"	Neut.	0.0018	0.0018	0	"
Morphine	HTr	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0	0	0	"
Veratrine	HTr	N/2	0.0049	0.0049	0	"
	"	N/4	0.0116	0.0116	0	"
	"	N/8	0.0112	0.0112	0	"
	"	Neut.	0.0294	0.0294	0	"

Table B.

Owing to the solubility of tartaric acid in ether, it is impossible to say whether the salt is present in the ether in the free state or as salt, in the extraction from acid solution.

Alkaloid	Acid	Strength	Grams alkaloid in 20 cc Ether Total	Free	Salt	Indicator
Strychnine	HTr	N/2	0	0	0	Azolitmin
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0	0	0	"
	Sulph.	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0.0027	0	0.0027	"
Brucine	HTr	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0.0040	?	?	"
	"	Neut.	0.0032	0.0032	0	"
	Sulph.	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0	0	0	"
Cinchonidine	HTr	N/2	0.0018	?	?	"
	"	N/4	0.0018	?	?	"
	"	N/8	0	0	0	"
	"	Neut.	0.0024	0.0012	0.0012	"
	Sulph.	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0.0040	0.0040	0	"
Cinchonine	HTr	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0.0014	?	?	"
	"	Neut.	0.0023	0.0023	0	"
Codeine	HTr	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0	0	0	"
	Sulpn.	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0.0023	0	0.0023	"
	"	Neut.	0	0	0	"

Table B. (continued)

Alkaloid	Acid	Strength	Grams alkaloid in 20 cc Ether: Total	Free	Salt	Indicator
Aconitine	HTr	N/2	0	0	0	Cochineal
	"	N/4	0	0	0	"
	"	N/8	0.0052	?	?	"
	"	Neut.	0.0060	0	0.0060	"
Atropine	HTr	N/2	0	0	0	"
	"	N/4	0.0011	?	?	"
	"	N/8	0.0014	?	?	"
	"	Neut.	0.0021	0	0.0021	"
Morphine	HTr	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0	0	0	"
	Sulph.	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0.0011	0.0011	0	"
	"	Neut.	0.0019	0.0019	0	"
Quinine	HTr	N/2	0	0	0	Azolitmin
	"	N/4	0	0	0	"
	"	N/8	0.0014	?	?	"
	Sulph.	N/2	0	0	0	"
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0	0	0	"
Veratrine	HTr	N/2	0	0	0	Cochineal
	"	N/4	0	0	0	"
	"	N/8	0	0	0	"
	"	Neut.	0.0024	0.0024	0	"

2- Conditions at equilibrium in systems in which the alkaloid is being removed from its chloroform solution by an acid.

0.2 gram of the alkaloid were dissolved in 20 cc of chloroform and 25 cc of the required concentration of acid added. The mixture was shaken for two hours and a half, in the same manner as in the previous case, at 25°. After separation of the two layers, the amount of alkaloid and alkaloidal salt in the chloroform layer was determined. The results are tabulated in Table C. Owing to the insolubility of some of the alkaloids in ether, values were not obtained for the use of this solvent. The chloroform solutions of the alkaloids were shaken out with sulphuric, hydrochloric and tartaric acids of the concentrations, N/2, N/4, N/8. In the case of Strychnine even more dilute acid solutions were used. In those cases where the salt formed is but slowly soluble in the acids, experiments were made to determine how many shakings would more quickly dissolve the salt, and what strength acid would be best.

Table C

Alkaloid	Nature Volume Acid	Strength	Grams alkaloid in 20cc Chloroform Total	Free	Salt	Indicator
Aconitine	HTr 25cc	N/2	0	0	0	Cochineal
	" 50cc	N/4	0	0	0	"
	" "	N/8	0	0	0	"
	HCl 25cc	N/2	0.0342	0	0.0342	"
	" "	N/4	0.0257	0	0.0257	"
	" "	N/8	0.0146	0	0.0146	"
Atropine	HTr 25cc	N/4	0.0010	0.0010	0	"
	" "	N/8	0.0010	0.0010	0	"
Brucine	HTr 25cc	N/2	0	0	0	Azolitmin
	" "	N/4	0	0	0	"
	" "	N/8	0.0014	0.0014	0	"
	" 35cc	N/8	0	0	0	"
	Sulph.25c	N/2	0	0	0	"
	" "	N/4	0.0008	0.0008	0	"
	" "	N/8	0.0012	0.0012	0	"
	HCl 25cc	N/2	0.0768	0	0.0768	"
	" "	N/4	0.0583	0	0.0583	"
	" "	N/8	0.0445	0	0.0445	"
Cinchonidine	HTr 25cc	N/2	0	0	0	"
	" 50cc	N/4	0	0	0	"
	" "	N/8	0	0	0	"
	Sulpn.25cc	N/2	0	0	0	"
	" ""	N/4	0	0	0	"
	" "	N/8	0.0012	0.0012	0	"
	HCl 25cc	N/2	0	0	0	"
	" "	N/4	0	0	0	"
	" "	N/8	0	0	0	"
Cinchonine	HTr 25cc	N/2	0	0	0	"
	" "	N/4	0	0	0	"
	" "	N/8	0	0	0	"
	Sulph.25cc	N/2	0	0	0	"
	" "	N/4	0	0	0	"
	" "	N/8	0.0011	0.0011	0	"
	HCl 25cc	N/2	0	0	0	"
	" "	N/4	0	0	0	"
	" "	N/8	0	0	0	"

Table C (continued)

Alkaloid	Nature Acid	Volume	Strength	Grams alkaloid in 20cc Chloroform Total	Free	Salt	Indicator
Cocaine	HTr	25cc	N/2	0	0	0	Cochineal
	"	"	N/4	0	0	0	"
	"	"	N/8	0.0017	0.0017	0	"
	Sulph.	25cc	N/2	0	0	0	"
	"	"	N/4	0	0	0	"
	"	"	N/8	0	0	0	"
	HCl	25cc	N/2	0	0	0	"
	"	"	N/4	0	0	0	"
	"	"	N/8	0	0	0	"
Codeine	HTr	25cc	N/2	0	0	0	Azolitmin
	"	"	N/4	0	0	0	"
	"	"	N/8	0	0	0	"
	Sulph.	25cc	N/2	0	0	0	"
	"	"	N/4	0	0	0	"
	"	"	N/8	0	0	0	"
	HCl	25cc	N/2	0	0	0	"
	"	"	N/4	0	0	0	"
	"	"	N/8	0	0	0	"
Quinine	HTr	25cc	N/2	0	0	0	"
	"	"	N/4	0	0	0	"
	"	"	N/8	0	0	0	"
	Sulph.	25cc	N/2	0	0	0	"
	"	"	N/4	0	0	0	"
	"	"	N/8	0	0	0	"
	HCl	25cc	N/2	0	0	0	"
	"	"	N/4	0	0	0	"
	"	"	N/8	0	0	0	"
Strychnine	HTr	50cc	4N	0	0	0	"
	"	100cc	2N	0	0	0	"
	"	100cc	N	0.0011	0	0.0011	"
	"	100cc	N/2	0.0011	0	0.0011	"
	"	95cc	N/4	0.0011	0	0.0011	"
	"	75cc	N/8	0.0011	0	0.0011	"
	"	75cc	N/12	0.0029	0	0.0029	"
	"	25cc	N/25	0.0125	0	0.0125	"
	HCl	25cc	N/2	0.0202	0	0.0202	"
	"	"	N/4	0.0250	0	0.0250	"
	"	"	N/8	0.0202	0	0.0202	"

Table C (continued)

Alkaloid	Nature Volume Acid		Strength	Grams alkaloid in 20cc Chloroform Total	Free	Salt	Indicator
Veratrine	HTr	25cc	N/2	0.0020	0.0020	0.0020	Cochineal
	"	"	N/4	0.0040	0.0040	0	"
	"	"	N/8	0	0	0	"
	Sulph.	25cc	N/2	0	0	0	"
	"	"	N/4	0	0	0	"
	"	"	N/8	0	0	0	"
	HCl	25cc	N/2	0.0740	0	0.0740	"
	"	"	N/4	0.0516	0	0.0516	"
	"	"	N/8	0.0426	0	0.0426	"

c) Calculation of the EXTRACTION FACTORS under the various equilibrium conditions examined, as well as those reported in the literature.

The 'extraction factor' is simply the ratio of the amount of alkaloid found in the layer of the added solvent to the amount originally present in the first solution, regardless of the volumes of the two solutions. This gives an excellent idea of the effeciency of the different sets of extraction conditions.

Table D contains the data and values for the extraction factors for the alkaloidal tartrates between tartaric acid and chloroform. In Table E will be found similar values where ether has been used as the solvent. The extraction factors for the sulphates between sulphuric acid and chloroform and of the hydrochlorides between hydrochloric acid and chloroform are found in Tables F and G, respectively. Table H contains the values, using ether for the solvent, for the sulphates.

The extraction factors for the extraction of the alkaloids from their chloroform solutions, by tartaric, sulphuric and hydrochloric acids will be found in Table I.

Table D

Alkaloid	Acid	Strength	Chloroform Volume	Chloroform Alkaloid	Acid Volume	Original Total Alkaloid	Factor
Strycnnine	HTr	N/2	20	0	25	0.1650	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0.0104	25	"	0.0634
	"	Neut.	20	0.0126	25	"	0.0763
Brucine	HTr	N/2	20	0	25	0.1680	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0.0026	25	"	0.0154
	"	Neut.	20	0.0076	25	"	0.0453
Cinchonidine	HTr	N/2	20	0.0012	25	0.1595	0.0076
	"	N/4	20	0.0024	25	"	0.0153
	"	N/8	20	0.0018	25	"	0.0114
	"	Neut.	20	0.0024	25	"	0.0153
Cinchonine	HTr	N/2	20	0	25	0.1595	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0	25	"	0
	"	Neut.	20	0.0016	25	"	0.0100
Quinine	HTr	N/2	20	0.0014	25	0.1625	0.0086
	"	N/4	20	0.0028	25	"	0.0172
	"	N/8	20	0.0028	25	"	0.0172
Aconitine	HTr	N/2	20	0	25	0.1930	0
	"	N/4	20	0.0053	25	"	0.0274
	"	N/8	20	0.0099	25	"	0.0512
	"	Neut.	20	0.0236	25	"	0.1240
Atropine	HTr	N/2	20	0	25	0.1585	0
	"	N/4	20	0.0036	25	"	0.0217
	"	N/8	20	0.0039	25	"	0.0245
	"	Neut.	20	0.0018	25	"	0.0108
Codeine	HTr	N/2	20	0	25	0.1600	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0.0018	25	"	0.0116
	"	Neut.	20	0.0046	25	"	0.0286
Morphine	HTr	N/2	20	0	25	0.1585	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0	25	"	0
	"	Neut.	20	0	25	"	0
Veratrine	HTr	N/2	20	0.0049	25	0.1775	0.0276
	"	N/4	20	0.0116	25	"	0.0645
	"	N/8	20	0.0112	25	"	0.0630
	"	Neut.	20	0.0294	25	"	0.1655

Table E

Alkaloid	Acid	Strength	Ether Volume	Ether Alkaloid	Acid Volume	Original Total Alkaloid	Factor
Strychnine	HTr	N/2	20	0	25	0.1640	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0	25	"	0
	"	Neut.	20	0	25	"	0
Brucine	HTr	N/2	20	0	25	0.1680	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0.0040	25	"	0.0238
	"	Neut.	20	0.0032	25	"	0.0191
Morphine	HTr	N/2	20	0	25	0.1585	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0	25	"	0
	"	Neut.	20	0	25	"	0
Cinchonidine	HTr	N/2	20	0.0018	25	0.1595	0.0114
	"	N/4	20	0.0018	25	"	0.0114
	"	N/8	20	0	25	"	0
	"	Neut.	20	0.0024	25	"	0.0153
Cinchonine	HTr	N/2	20	0	25	0.1595	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0.0014	25	"	0.0087
	"	Neut.	20	0.0023	25	"	0.0144
Quinine	HTr	N/2	20	0	25	0.1625	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0.0014	25	"	0.0086
Codeine	HTr	N/2	20	0	25	0.1600	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0	25	"	0
	"	Neut.	20	0	25	"	0
Aconitine	HTr	N/2	20	0	25	0.1930	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0.0052	25	"	0.0269
	"	Neut.	20	0.0060	25	"	0.0310
Atropine	HTr	N/2	20	0	25	0.1585	0
	"	N/4	20	0.0011	25	"	0.0069
	"	N/8	20	0.0014	25	"	0.0088
	"	Neut.	20	0.0021	25	"	0.0132
Veratrine	HTr	N/2	20	0	25	0.1775	0
	"	N/4	20	0	25	"	0
	"	N/8	20	0	25	"	0
	"	Neut.	20	0.0024	25	"	0.0135

Table F

Alkaloid	Sulphuric Acid Strength	Chloroform Volume	Acid Alkaloid	Acid Volume	Total Alkaloid	Extraction Factor	References
Strychnine	N/2	20	0	25	0.1745	0	Authors
	N/4	20	0	25	"	0	"
	N/8	20	0	25	"	0	"
	N/50	20	0	25	"	0	"
	Neut.	20	0.0127	25	"	0.0727	"
	.17N	50	Traces	70	0.2000	0	Kippenberger
	1%	50?	Traces	50	0.2610	0	Simmer
	Neut.	50?	Traces	50	"	0	"
Brucine	N/2	20	0	25	0.1780	0	Authors
	N/4	20	0	25	"	0	"
	N/8	20	0	25	"	0	"
	Neut.	20	0.0143	25	"	0.0803	"
	.17N	50	0.0020	70	0.2000	0.0100	Kippenberger
Cinchonidine	N/2	20	0	25	0.1715	0	Authors
	N/4	20	0	25	"	0	"
	N/8	20	0	25	"	0	"
	Neut.	20	0.0086	25	"	0.0503	"
Quinine	N/2	20	0	25	0.1740	0	"
	N/4	20	0	25	"	0	"
	N/8	20	00	25	"	0	"
	Neut.	20	0	25	"	0	"
	.034N	50	0	70	0.2000	0	Kippenberger
Atropine	.034N	50	0	70	0.2000	0	"
	Neut.	50	0.0010	70	"	0.0050	"
Morphine	.034N	50	0	70	0.2000	0	"
Aconitine	.255N	50	Traces	70	0.2000	0	"
	.085N	50	0.0064	70	0.2000	0.0320	"
	.017N	50	0.0130	70	0.2000	0.0650	"
Veratrine	.017N	50	Traces	70	0.2000	0	"
	N/49	50?	Traces	50	0.2150	0	Simmer
	Neut.	50?	0.0374	50	"	0.1780	"
Codeine	.034N	50	0	70	0.2000	0	Kippenberger
	N/49	50?	Traces	50	0.2470	0	Simmer
	Neut.	50?	0.0276	50	"	0.1116	"
Cocaine	.255N	50	0	70	0.2000	0	Kippenberger
	.017N	50	Traces	70	"	0	"
	Neut.	50?	0.0143	50	0.2640	0.0540	Simmer

Table G

Alkaloid	Acid- Hydrochloric Acid - Chloroform Volume Strength		Acid Volume Alkaloid		Total Alkaloid	Extraction Factor	References
Strychnine	N/2	20	0.0522	25	0.180	0.2895	Authors
	N/4	20	0.0424	25	"	0.2360	"
	N/8	20	0.0394	25	"	0.2182	"
	Neut.	20	0.0085	25	"	0.0472	"
	N/6.75	50	0.0920	70	0.200	0.4600	Kippenberger
	6.85N	50?	0.0233	50	0.2377	0.1020	Simmer
	2.74N	50?	0.0559	50	"	0.2360	"
	.274N	50?	0.0250	50	"	0.1050	"
	.027N	50?	0.0083	50	"	0.0340	"
	Neut	50?	0.0158	50	"	0.0665	"
Brucine	.075N	50	0.0898	70	0.2000	0.4490	Kippenberger
Cocaine	N/2	20	0	25	0.1790	0	Authors
	N/4	20	0	25	"	0	"
	N/8	20	0.0432	25	"	0.2420	"
	Neut.	20	0.0432	25	"	0.2420	"
	2.74N	50?	0.0075	50	0.2240	0.0335	Simmer
	.274N	50?	0.0045	50	"	0.0210	"
	.027N	50?	0.0037	50	"	0.0165	"
	Neut	50?	0.0490	50	"	0.4900	"
	.017N	100	0.0021	70	0.2000	0.0110	Kippenberger
Atropine	.075N	50	0.0014	70	0.2000	0.0070	"
	2.74N	50?	0.0028	50	0.2250	0.0124	Simmer
	.027N	50?	0	50	"	0	"
	Neut.	50?	0	50	"	0	"
Morphine	.075N	50	0	70	0.2000	0	Kippenberger
	1.37N	50?	0	50	0.2470	0	Simmer
	.027N	50?	0	50	"	0	"
	Neut.	50?	0.0045	50	"	0.0182	"
Aconitine	.030N	50	0.0971	70	0.2000	0.4850	Kippenberger
Veratrine	.075N	50	0.0807	70	0.2000	0.4035	"
	2.74N	50?	0.1248	50	0.2110	0.5920	Simmer
	.027N	50?	0.0327	50	0.2110	0.1550	"
	Neut.	50?	0.0530	50	0.2110	0.2520	"
Codeine	.030N	50	Traces	70	0.2000	0	Kippenberger
	2.74N	50?	0.0079	50	0.2340	0.0338	Simmer
	.027N	50?	0.0015	50	"	0.0064	"
	Neut.	50?	0.0371	50	"	0.0158	"

Table H

Acid- Sulphuric Acid - Alkaloid	Acid Strength	Ether Volume	Alkaloid	Acid Volume	Original Total Alkaloid	Extraction Factor
Strychnine	N/2	20	0	25	0.1745	0
	N/4	20	0	25	"	0
	N/8	20	0	25	"	0
	Neut.	20	0.0027	25	"	0.0155
Brucine	N/2	20	0	25	0.1780	0
	N/4	20	0	25	"	0
	N/8	20	0	25	"	0
	Neut.	20	0	25	"	0
Morphine	N/2	20	0	25	0.1730	0
	N/4	20	0	25	"	0
	N/8	20	0.0011	25	"	0.0063
	Neut.	20	0.0019	25	"	0.0110
Cinchonidine	N/2	20	0	25	0.1715	0
	N/4	20	0	25	"	0
	N/8	20	0	25	"	0
	Neut.	20	0.0040	25	"	0.0237
Quinine	N/2	20	0	25	0.1740	0
	N/4	20	0	25	"	0
	N/8	20	0	25	"	0
	Neut.	20	0	25	"	0
Codeine	N/2	20	0	25	0.1720	0
	N/4	20	0	25	"	0
	N/8	20	0.0024	25	"	0.0139
	Neut.	20	0	25	"	0

Table I

Alkaloid	Acid	Strength	Chloroform Volume	Original Alkaloid	Acid Volume	Weight in Acid Alkaloid	Ext'n Factor
Aconitine	HTr	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	50	0.200	1.00
	"	N/8	20	0.200	50	0.200	1.00
	HCl	N/2	20	0.200	25	0.165	0.830
	"	N/4	20	0.200	25	0.174	0.872
	"	N/8	20	0.200	25	0.186	0.930
Atropine	HTr	N/4	20	0.150	25	0.149	0.994
	"	N/8	20	0.200	25	0.199	0.996
Brucine	HTr	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.192	0.964
	"	N/8	20	0.200	25	0.200	1.00
	Sulph.	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.199	0.996
	"	N/8	20	0.200	25	0.198	0.994
	HCl	N/2	20	0.200	25	0.1232	0.617
	"	N/4	20	0.200	25	0.1417	0.708
	"	N/8	20	0.200	25	0.1555	0.777
Cinchonidine	HTr	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	50	0.200	1.00
	"	N/8	20	0.200	50	0.200	1.00
	Sulph.	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.198	0.995
	HCl	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00
Cinchonine	HTr	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00
	Sulph.	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.1998	0.995
	HCl	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00

Table I (continued)

Alkaloid	Acid	Strength	Chloroform Volume	Original Alkaloid	Acid Volume	Weight Alkaloid	Ext'n Factor
Cocaine	HTr	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.198	0.990
	Sulph.	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00
	HCl	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00
Codeine	HTr	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00
	Sulph.	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00
	HCl	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00
Quinine	HTr	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00
	Sulph.	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00
	HCl	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00
Strychnine	HTr	4N	20	0.200	50	0.200	1.00
	"	2N	20	0.200	100	0.200	1.00
	"	N	20	0.200	100	0.198	0.996
	"	N/2	20	0.200	100	0.198	0.996
	"	N/4	20	0.200	95	0.198	0.996
	"	N/8	20	0.200	75	0.198	0.996
	"	N/12	20	0.200	75	0.197	0.986
	"	N/25	20	0.200	25	0.187	0.938
	HCl	N/2	20	0.200	25	0.179	0.900
	"	N/4	20	0.200	25	0.175	0.875
	"	N/8	20	0.200	25	0.179	0.899

Table I (continued)

Alkaloid	Acid	Strength	Chloroform Volume	Original Alkaloid	Acid Volume	Weight Alkaloid	Extr'n Factor
Veratrine	Htr	N/2	20	0.200	25	0.198	0.990
	"	N/4	20	0.200	25	0.196	0.980
	"	N/8	20	0.200	25	0.200	1.00
	Sulph.	N/2	20	0.200	25	0.200	1.00
	"	N/4	20	0.200	25	0.200	1.00
	"	N/8	20	0.200	25	0.200	1.00
	HCl	N/2	20	0.200	25	0.126	0.630
	"	N/4	20	0.200	25	0.148	0.742
	"	N/8	20	0.200	25	0.157	0.787

V- Discussion of Results.

In looking over the tables, the following results will be observed.

Aconitine

In the washing of a solution of aconitine tartrate with chloroform, it is seen that the more concentrated the acid is, the less alkaloid will be removed. Hydrolysis takes place in the neutral solution with the removal of about 11% of the alkaloid in the free state. Whatever alkaloid is removed from the acid solution is removed in the form of salt and not in the free state. Aconitine is also removed from solution in sulphuric acid, provided the acid is less than N/4 concentration, but in much smaller amounts than from tartaric acid. From hydrochloric acid solution, the amount of alkaloid removed is in direct proportion to the strength of the acid and the alkaloid is almost entirely removed as the salt, showing that hydrochloric acid is a fairly good solvent for the hydrochloride salts of Aconitine.

Atropine

The same phenomena will be observed in the cases of the sulphates and tartrates of Atropine, namely that as acidity increases, less alkaloid will be removed by ether or chloroform. With the hydrochlorides, it is reversed, and as the strength of the acid increases, the amount of alkaloid removed increases, and it is removed as the salt.

Brucine

Brucine is not removed from tartaric acid solutions of

strength greater than N/4 by either chloroform or ether, although with a decrease in the concentration of the acid from that point down, there is increased hydrolytic action with the removal of the alkaloid in the uncombined state. Sulphuric acid retains the alkaloid from removal by either chloroform or ether from acid solution and ether does not even extract any from the neutral solution. From a 0.075 N solution of the hydrochloride in hydrochloric acid, 45% of the alkaloid is removed by chloroform and most of it as the salt.

Cinchonidine and Cinchonine

Cinchonidine, Cinchonine, and Quinine differ from the other alkaloids in that their hydrochloride salts are insoluble in chloroform. Many of the hydrochlorides of the other alkaloids are soluble to a great extent in this solvent. The neutral tartrates and sulphates are hydrolysed and the alkaloids removed by both ether and chloroform. Cinchonidine differs from Cinchonine in that the tartrates are hydrolysed in acid solution and some of the alkaloid removed as free Cinchonidine.

Quinine

Quinine sulphate is neither hydrolysed in neutral and acid solution nor is the salt soluble in either ether or chloroform. The neutral tartrate is only slightly soluble in water, but the N/8 acid solution is hydrolysed to a slight extent, giving up quinine in both the free and combined condition to chloroform and in the free state to ether.

Morphine

Neither chloroform nor ether remove Morphine from the

neutral or acid solution of the tartrate. The neutral sulphate is slightly hydrolysed and some free Morphine found in the ether.

Strychnine

Hydrolytic action takes place in the N/8 tartaric acid and neutral solution of the strychnine tartrate and some alkaloid is removed by the chloroform in the free state. Increase in acidity with both the sulphates and tartrates causes a decrease in the amount of alkaloid removed; the reverse being true in the case of the hydrochlorides.

Veratrine

Veratrine is removed in appreciable amounts from the tartaric acid solution by chloroform, but only from the neutral solution by ether. Chloroform does not take up any of the alkaloid from the sulphuric acid but appreciably lowers the concentration of the alkaloid in the hydrochloric acid solutions.

Codeine

Neither ether nor chloroform will remove codeine from solution in N/2 or N/4 tartaric acid but chloroform removes increasing amounts as the concentration of the acid decreases from that point on. The hydrochlorides are more soluble in chloroform the greater the concentration of the acid. Hydrolysis takes place in the neutral solutions and much codeine is removed.

In general, the following principles may be apparent in the foregoing:

1- The neutral sulphates and tartrates in aqueous solution are hydrolysed to a certain extent with the subsequent formation of free alkaloid and acid. This alkaloid may be removed by the immiscible solvent.

2- With an increase in the acidity of the solution, the hydrolytic action becomes less and the amount of alkaloid taken up in the free state decreases with the increase in acidity.

3- Many of the acid sulphates and tartrates are removed as salts to a slight degree, by chloroform and ether.

4- The alkaloidal hydrochlorides tend to be quite soluble in chloroform and in such cases, the solubility increases with the acidity of the solution, in all the cases studied.

By means of this data, the following questions may be answered:

1 What conditions of acidity would completely remove the alkaloid from its chloroform solution?

2- Which solvent, chloroform or ether, can best be used for shaking out the neutral or acid solution of the alkaloidal tartrates or sulphates, without removing the alkaloid?

3- And which salts are least easily removed by chloroform or ether, and in what concentration of acid, either by hydrolysis or through the solubility of the salt itself in the immiscible solvent?

1- The best conditions of acidity for completely removing the alkaloids from the chloroform solution. The following chart gives the values for the extraction of 0.2 gram of the alkaloid from 20 cc of the solvent chloroform, by the different acids.

Alkaloid	Acid	Strength	Volume
Aconitine	HTr	N/8	2 portions of 25 cc each
Atropine	HTr	N/8	1 portion of 25 and 1 of 10 cc
Brucine	HTr	N/8	" " " " " " " "
Cinchonidine and Cinchonine	HCl	N/8	25 cc
	Sulph.	N/8	1 portion of 25 and 1 of 10 cc
Cocaine and Codeine	Sulph.	N/8	25 cc
	HCl	N/8	25 cc
Quinine	HCl	N/8	25 cc
	HTr	"	25 cc
	Sulph.	"	25 cc
Strychnine	HTr	N/8	3 portions of 25 cc each.
Veratrine	HTr	N/8	25 cc
	Sulph.	"	25 cc

2- The best solvent for shaking out the neutral and acid solutions of the alkaloidal tartrates, without the loss of alkaloid.

Alkaloid	Solvent	Strength HTr	% Alkaloid removed
Aconitine	Ether	N/4	0
Atropine	Chloroform	Slightly acid	1.0
Brucine	Chloroform	N/8	1.5
Cinchonidine	Ether	Slightly acid	1.2
Cinchonine	Chloroform	N/8	0
Codeine	Ether	N/8	0
Quinine	Ether	N/8	0.8
Morphine	Either one	Slightly acid	0
Strychnine	Ether	" "	0
Veratrine	Ether	N/8	0

3- The salts that are least easily removed by chloroform or ether and the best concentration of acid.

	Chloroform			Ether		
Alkaloid	Salts	Strength Acid	% Removed	Salts	Strength Acid	% Removed
Aconitine	Sulphate	N/4	0	Tartrate	N/4	0
	Tartrate	"	0			
Atropine	HCl	0.02N	0	Sulphate	N/10	0
Brucine	Sulphate	N/8	0	Sulphate	N/10	0
Cinchonine	Tartrate	N/8	0	Tartrate	N/8	0.8
Cinchonidine	Sulphate	N/8	0	Tartrate	N/8	0
Codeine	Sulphate	N/50	0	Sulphate	N/10	0
Quinine	Sulphate	N/50	0	Sulphate	N/10	0
Morphine	Sulphate	N/50	0	Tartrate	N/8	0
Strychnine	Sulphate	N/50	0	Tartrate	N/8	0
Veratrine	Sulphate	N/50	0	Tartrate	N/8	0

In addition, calculations may be made which will tell how many shakings from chloroform solution need be made by an acid to completely remove the alkaloid from the chloroform solution. If 94% of the alkaloid is removed in the first shaking with 25 cc of acid, the second extraction will remove 94% of the 6% left, or 5.86%. Thus these two extractions will remove 99.86% of the alkaloid. A third extraction will take take away 94% of the remaining 0.14% or 0.131% so the three extractions with the acid will make practically a complete removal.

The following table shows the number of shakings necessary to remove 0.2 gram of alkaloid from 20 cc of a chloroform solution.

Alkaloid	Acid	Strength	% Alkaloid removed in 1st shaking	Number of shakings for complete removal.	Total acid volume
Aconitine	HTr	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
	HCl	N/2	83.0	4	100
	"	N/4	87.2	3	75
	"	N/8	93.0	3	75
Atropine	HTr	N/4	99.4	2	35
	"	N/8	99.6	2	35
Brucine	HTr	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	96.4	2	35
	Sulpn.	N/2	100.	1	25
	"	N/4	99.6	2	35
	"	N/8	99.4	2	35
	HCl	N/2	61.7	6	150
	"	N/4	70.8	5	125
	"	N/8	77.7	4	100
Cinchonidine	HTr	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
	HCl	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
	Sulph.	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	99.5	2	35
Cinchonine	HTr	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
	HCl	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
	Sulph.	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	99.8	2	35
Cocaine	HTr	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	99.0	2	35

Alkaloid	Acid	Strength	% alkaloid removed in 1st shaking	Number of shakings for complete removal	Total acid volume
Cocaine	Sulpn.	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
	HCl	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
Codeine	HTr	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
	Sulph.	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
	HCl	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
Quinine	HTr	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
	Sulph.	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
	HCl	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25
Strychnine	HTr	4N	100. after 2 shakings of 25 cc each		
	"	2N	100. after 4 shakings of 25 cc each		
	"	N	99.6 after 4 shakings of 25 cc each		
	"	N/2	99.6 after 4 shakings of 25 cc each		
	"	N/4	99.6 after 4 shakings (3x25 plus 10 cc)		
	"	N/8	99.6 after 3 shakings of 25 cc each		
	"	N/12	98.6 after 3 shakings of 25 cc each		
	"	N/25	93.8 after 1 shaking of 25 cc		
	For complete removal by N/25 acid, 2 shakings.				
	HCl	N/2	90.0	3	75
	"	N/4	87.5	3	75
	"	N/8	89.9	3	75
Veratrine	HTr	N/2	99.0	2	35
	"	N/4	98.0	2	35
	"	N/8	100.0	1	25

Alkaloid	Acid	Strength	% Alkaloid removed in 1st shaking	Number of shakings for complete removal	Total Acid Volume
Veratrine	HCl	N/2	63.0	6	150
	"	N/4	74.2	5	125
	"	N/8	78.7	4	100
	Sulph.	N/2	100.	1	25
	"	N/4	100.	1	25
	"	N/8	100.	1	25

VI- Summary

1- The most practical method for the determination of alkaloids involves the extraction of the alkaloid from an aqueous solution by means of an immiscible solvent such as chloroform or ether.

2- It further involves the purification of the alkaloidal solution by removal of gums, colors, etc, by similar methods.

3- Unless conditions are carefully guarded, loss of alkaloid as salt or in the free state will occur during the extraction.

4- The equilibrium conditions for the following systems have been established, in the case of the alkaloids Aconitine, Atropine, Brucine, Cinchonidine, Cinchonine, Cocaine, Codeine, Morphine, Quinine, Strychnine, and Veratrine:

a- The alkaloidal tartrates, tartaric acid, water and chloroform.

b- The alkaloidal tartrates, tartaric acid, water and ether.

c- Certain alkaloidal sulphates, sulphuric acid, water, and chloroform.

d- Certain alkaloidal sulphates, sulphuric acid, water, and ether.

e- Certain alkaloidal hydrochlorides, hydrochloric acid, water, and chloroform.

f- The Extraction Factors have been determined for all these systems, as well as those described in the literature, and the most favorable conditions for extraction calculated.

Index

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